General

Guideline Title

ACR Appropriateness Criteria® thyroid carcinoma.

Bibliographic Source(s)

Salama JK, Golden DW, Beitler JJ, Yom SS, Garg MK, Lawson J, McDonald MW, Quon H, Ridge JA, Saba N, Smith RV, Worden F, Yeung AR, Expert Panel on Radiation Oncologyâ€“Head & Neck Cancer. ACR Appropriateness CriteriaÂ® thyroid carcinoma. [online publication]. Reston (VA): American College of Radiology (ACR); 2013. 18 p. [100 references]

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

ACR Appropriateness Criteria®

Clinical Condition: Thyroid Carcinoma

Variant 1: T1a N0 M0 papillary thyroid cancer: 40-year-old woman.

Treatment	Rating	Comments
Total lobectomy (hemithyroidectomy)	8	
Total thyroidectomy	8	
Thyroglobulin suppression with levothyroxine	9	
Postoperative Adjuvant Radioactive Iodine (RRA or RAI)		
30 mCi with thyrotropin stimulation	3	
100 mCi with thyrotropin stimulation	1	
30 mCi with thyroid hormone withdrawal	2	

Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate

Treatment	Rating	Comments
withdrawal		
Postoperative external beam radiotherapy	1	
Postoperative chemotherapy	1	
Adjuvant concurrent chemoradiotherapy	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 2: T1b N0 M0 papillary thyroid carcinoma: 60-year-old man.

Treatment	Rating	Comments
Total lobectomy (hemithyroidectomy)	3	
Total thyroidectomy	9	
Thyroglobulin suppression with levothyroxine	9	
Postoperative Adjuvant Radioactive Iodine (RRA or RAI)		
30 mCi with thyrotropin stimulation	5	Depends on final pathology and post-treatment evaluation.
100 mCi with thyrotropin stimulation	7	Many patients will not require this high of a dose.
30 mCi with thyroid hormone withdrawal	4	Associated with worse side effects than thyrotropin stimulation.
100 mCi with thyroid hormone withdrawal	6	Depends on final pathology and post-treatment evaluation. Many patients may not require this high of a dose. Associated with worse side effects than thyrotropin stimulation.
Postoperative external beam radiotherapy	1	
Postoperative chemotherapy	1	
Adjuvant concurrent chemoradiotherapy	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 3: T4a N1a M0 papillary thyroid carcinoma: 65-year-old man.

Treatment	Rating	Comments
Total lobectomy (hemithyroidectomy)	1	
Total thyroidectomy	9	
Thyroglobulin suppression with levothyroxine	9	
Postoperative Adjuvant Radioactive Iodine (RRA or RAI)		
30 mCi with thyrotropin stimulation	1	
100 mCi with thyrotropin stimulation	8	
30 mCi with thyroid hormone withdrawal	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Treatment	Rating	Comments
100 mCi with thyroid hormone withdrawal	7	
Postoperative External Beam Radiotherapy		
3D-CRT	5	
IMRT	8	
Treat thyroid bed first echelon LNs only	5	
Treat thyroid bed and entire elective neck	8	
Postoperative chemotherapy	1	
Adjuvant concurrent chemoradiotherapy	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 4: T4a N0 M0 medullary thyroid carcinoma: 28-year-old woman.

Treatment	Rating	Comments
Total lobectomy (hemithyroidectomy)	1	
Total thyroidectomy with neck dissection	8	
Thyroglobulin suppression with levothyroxine	1	
Postoperative Adjuvant Radioactive Iodine (RRA or RAI)		
30 mCi (after total thyroidectomy)	1	
100 mCi (after subtotal thyroidectomy)	1	
200 mCi (after subtotal thyroidectomy)	1	
Postoperative adjuvant external beam radiotherapy	5	
Postoperative External Beam Radiotherapy Technique		
3D-CRT	5	
IMRT	8	
Postoperative chemotherapy	1	
Adjuvant concurrent chemoradiotherapy	1	
Genetic testing for family members	9	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 5: T4a N0 M0 anaplastic thyroid carcinoma: 64-year-old man with excellent performance status.

Treatment	Rating	Comments
Total lobectomy (hemithyroidectomy)	1	
Total thyroidectomy	7	
Lateral lymph node dissection	3	Assuming total thyroidectomy has been done.
Thyroglobulin suppression with levothyroxine	1	
Postoperative adjuvant radioactive iodine (RRA or RAI)	1	
External Beam Radiotherapy		
Postoperative concurrent chemoradiotherapy (if surgery indicated)	8	
Definitive chemoradiotherapy (if no surgery performed)	8	
Postoperative External Beam Radiotherapy Technique/Fractionation		
3D-CRT	6	
IMRT	8	
Altered fractionation	5	
Postoperative External Beam Radiotherapy Volume		
Treat thyroid/postoperative bed only	3	
Treat thyroid/postoperative bed and elective neck	8	
Palliative chemotherapy alone	2	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 6: T4b N1b M0 anaplastic thyroid carcinoma: 58-year-old woman with excellent performance status.

Treatment	Rating	Comments
Total lobectomy (hemithyroidectomy)	3	
Total thyroidectomy	1	
Lymph node dissection	2	
Thyroglobulin suppression with levothyroxine	1	
Postoperative radioactive iodine (RRA or RAI)	1	
External Beam Radiotherapy		
Definitive concurrent chemoradiotherapy	9	
External Beam Radiotherapy Technique/Fractionation		
3D-CRT	5	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Treatment	Rating	Comments
IMRT	7	
Altered fractionation	5	
External Beam Radiotherapy Volume		
Treat thyroid/postoperative bed only	1	
Treat thyroid/postoperative bed and elective neck	8	
Palliative chemotherapy alone	2	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 7: T4a N1 M1 papillary thyroid carcinoma: 63-year-old man with excellent performance status and lung micronodules.

Treatment	Rating	Comments
Total thyroidectomy	8	
Postoperative radioactive iodine	8	
Postoperative external beam radiotherapy	5	
RAI		
150 mCi	7	
200 mCi	6	
Adjuvant concurrent chemoradiation	2	
Cytotoxic chemotherapy	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 8: T3 N0 M1 papillary thyroid carcinoma: 40-year-old woman with excellent performance status and painful bony metastases; tumor is not iodine-avid.

Treatment	Rating	Comments
Palliative external beam radiotherapy	8	
Tyrosine kinase inhibitor (TKI) therapy	7	
Total thyroidectomy	5	
Cytotoxic chemotherapy	5	
Postoperative radioactive iodine	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Summary of Literature Review

Introduction/Background

Thyroid cancer is the most common endocrine malignancy in the United States, where the annual incidence is approximately 37,000 and increasing due to the more frequent diagnosis of early well-differentiated thyroid carcinoma (WDTC). Annually, approximately 1,600 people die from thyroid

malignancies. Women represent approximately 75% of newly diagnosed thyroid carcinoma cases. Risk factors for thyroid cancer include exposure to ionizing radiation and a family history of the disease. Thyroid cancer spans a spectrum of disease entities from the often curable, well-differentiated histologies (papillary, follicular/Hürthle cell, and medullary) to the aggressive anaplastic histology that represents only 2% of all thyroid cancer cases but 50% of thyroid cancer-related deaths. Guidelines for the management of thyroid carcinoma have been promulgated and are widely used. The overwhelming majority of patients with WDTC will do well with appropriate treatment. The high long-term survivorship and relative rarity of the disease have frustrated efforts to execute randomized trials, so management recommendations are not guided by conventional modern standards in oncology.

Anatomy and Physiology of the Thyroid Gland

The thyroid gland is a bilobed organ joined at the isthmus, which is located just inferior to the cricoid cartilage and surrounds the anterior portion of the trachea. The recurrent and superior laryngeal nerves pass near the thyroid gland on their way to the larynx. Four parathyroid glands are usually located near the thyroid gland as well.

The physiology of the thyroid gland is unique. Thyrotropin-releasing hormone, produced within the hypothalamus, signals the anterior pituitary to release thyroid-stimulating hormone (TSH). TSH then stimulates the follicular cells within the thyroid gland to release thyroxine, which in turn modulates the body's metabolic rate. Iodine is required for the production of thyroxine. The production of TSH and thyroxine is tightly regulated by a negative feedback loop within the hypothalamic-thalamic-thyroid axis. TSH can stimulate both normal thyrocytes and WDTC cells. Therefore, TSH suppression is a vital component of treatment for WDTC. The thyroid gland also contains parafollicular C cells that secrete calcitonin, a hormone that helps regulate, but is not mandatory for, calcium homeostasis. Primary lymphatic drainage of the thyroid is to the central neck compartment (level VI), with secondary echelons including the internal jugular chain (levels II–IV), posterior neck (level V), and superior mediastinum (level VII). However, this drainage pattern is inconsistent, and skip metastases directly to the lateral neck compartment have been reported in ≤20% of cases.

Presentation of Thyroid Carcinoma

A thyroid carcinoma most often presents as a localized palpable nodule, although the disease is increasingly detected as an incidental finding resulting from imaging studies conducted to evaluate other conditions. The cancer may present with lateral cervical lymphadenopathy from metastatic disease, compressive symptoms (including respiratory embarrassment and dysphagia), and hoarseness with recurrent laryngeal nerve injury. Fine needle aspiration biopsy represents the appropriate initial diagnostic maneuver, and it readily distinguishes many papillary thyroid carcinomas (PTCs), medullary thyroid carcinoma (MTC), and anaplastic thyroid carcinoma (ATC) from benign nodular thyroid disease. A benign follicular adenoma cannot be distinguished from a follicular carcinoma without examination of the lesion margin for vascular or capsular invasion. Hence, a thyroidectomy is required to confirm follicular thyroid cancer (FTC), which represents only about 20% of follicular neoplasms. The follicular variant of papillary carcinoma may also present with what appears to be a follicular neoplasm. The molecular mechanisms of malignant transformation include activating mutations in the RAS-RAF-MEK-ERK pathway in PTC, mutations in the RET proto-oncogene in MTC, and protein 53 defects in ATC.

Thyroid cancers typically spread to distant sites in a characteristic fashion, depending on the histology—PTC to lymph nodes, lungs, and bones; FTC to bones and lungs; and ATC to lymph nodes, lungs, bones, brain, and other sites. As many as 50% of patients with apparently localized PTC harbor lymph node metastases. Few develop a clinically significant progression in nodes. Unlike other FTC, Hürthle cell carcinomas (HCCs) may spread to regional lymph nodes. PTC often afflicts children and young adults, but it is a far more threatening malignancy in older individuals. Mortality rises with patient age.

Treatment of Thyroid Carcinoma

Surgery is the mainstay of treatment for WDTC, and the overwhelming majority of patients who undergo complete resection of their clinical disease will do well. Adjuvant treatment with radioactive iodine (RAI) using iodine-131 (^{131}I) is frequently used for diagnostic and therapeutic purposes. MTC, arising from C cells, is characterized by the early dissemination to lymph nodes and does not concentrate iodine. Resection should include a lymphadenectomy, the extent of which remains subject to debate. Most ATCs are unresectable at presentation. Surgical maneuvers (including tracheotomy) are controversial. Distant metastases are common, and chemoradiotherapy alone represents the usual management strategy.

WDTC includes PTC (the most common variant of thyroid cancer), FTC (which includes HCC), and MTC. The primary treatment modality for WDTC is surgery. For most WDTCs, a total thyroidectomy is recommended, although there is strong support for a total lobectomy for a substantial group of patients with low-risk disease (age 15–45 years, with no prior radiation, no distant metastases, no cervical nodal disease, no clinical or radiographic extrathyroidal extension, cancer <4 cm in diameter, and no aggressive variant). Although multiple studies have suggested improved outcomes with a total thyroidectomy compared with a partial thyroidectomy, controversy persists because the morbidity of bilateral

thyroidectomy is higher (particularly with respect to parathyroid injury) even in experienced hands. A series of 1,355 patients with PTC or FTC showed a 30-year recurrence rate of 40% after a subtotal thyroidectomy versus 26% after a total or near-total thyroidectomy. Furthermore, a total thyroidectomy is advantageous for several reasons: 1) follow-up screening for recurrence or metastasis is simplified if there is no residual thyroid tissue; 2) postoperative RAI is more effective when there is no residual normal thyroid tissue; and 3) completion thyroidectomy for recurrent disease has a high associated morbidity (due to the resulting total thyroidectomy, with increased risks to the laryngeal nerves and parathyroid glands).

Papillary microcarcinoma (<10 mm) is managed on a clinical spectrum from a subtotal thyroidectomy and no adjuvant treatment to a total thyroidectomy followed by RAI. In autopsy studies, an occult papillary microcarcinoma has been detected in ≤35% of specimens, indicating that this disease entity is unlikely to progress to clinically symptomatic PTC. Given the risks of a second malignancy and other toxicity associated with RAI, a total lobectomy or subtotal/total thyroidectomy without RAI is adequate treatment for papillary microcarcinoma.

Following surgery for WDTC, all patients should begin thyroxine supplementation with the goal of suppressing TSH production, as this can stimulate residual disease and/or metastatic progression. Some advocate for thyroxine supplementation even for microcarcinomas, although this method is controversial. Recommended goals for TSH suppression are <0.01–0.1 mU/L for high-risk patients and <0.1–0.4 mU/L for low-risk patients, with risk based on the aforementioned factors. Serum thyroglobulin should be monitored for evidence of recurrence or metastasis. Serial neck ultrasound and RAI diagnostic scans may be used to assess for recurrence. Postoperatively, risk factors should be assessed to determine whether the patient may benefit from RAI and external beam radiotherapy (EBRT).

Multiple prognostic systems have been developed, using factors that include patient age, tumor grade, extracapsular extension, tumor size, distant metastases, deoxyribonucleic acid (DNA) aneuploidy, completeness of resection, and extent of resection to determine the prognosis and possible benefit of adjuvant therapy. These prognostic systems are applicable in both PTC and FTC/HCC. Any imaging studies within 6 weeks of a planned RAI treatment should be done without intravenous contrast.

Well-Differentiated Thyroid Cancer—Iodine Avid

Indications for postoperative adjuvant RAI are: 1) tumor >1–1.5 cm; 2) patient age >45 years; 3) capsular, vascular, or soft-tissue invasion; 4) multifocal, residual, or recurrent disease; 5) lymph node metastasis; 6) distant metastasis; and 7) intermediate or high-risk disease based on a prognostic system. RAI is usually administered 4 to 12 weeks after a thyroidectomy. RAI without a known residual disease can ablate the microscopic local or distant disease. The RAI dose is usually 30 mCi for low-risk or 75 to 100 mCi for intermediate-risk disease. Higher doses of 150 to 200 mCi are administrated for patients at high risk for local recurrence, death from macroscopic disease, or with gross distant metastases. Because ^{131}I is cleared by the kidneys, the dose should be reduced for patients with impaired renal function or end-stage renal disease. RAI may be safely administered on an outpatient basis. RAI should not be given to pregnant women due to the theoretical risk to the fetus.

There are no randomized controlled trials investigating the use of RAI when there is no gross residual disease. Multiple retrospective studies and 1 meta-analysis have shown that ^{131}I ablation improves outcomes. However, other studies have failed to show a benefit. The Mayo Clinic found no difference in mortality or recurrence when it compared a cohort of patients treated in the era before ^{131}I use with a later cohort that received RAI in 50% of cases. Additionally, a more recent systematic review and meta-analysis failed to show a benefit for RAI in reducing recurrence or improving disease-specific mortality in low-risk patients. However, as the definition of low-risk patients frequently changes between studies, it is often difficult to identify groups that truly will or will not benefit from RAI. One multi-institutional series risk-stratified close to 3,000 patients as low risk (stage I), intermediate risk (stage II), and high risk (stages III–IV). In this study, a benefit of RAI use was seen in stages II–IV, but not stage I. Multiple studies have demonstrated a benefit of RAI use in patients with residual or high-risk disease. In 1 series, the treatment of residual tumor after surgery was associated with an approximately 50% decrease in local recurrence and disease-specific mortality. Based on these results, RAI should be considered in patients at stage II or higher or possibly in patients with any risk features at stage I.

In 1 review of a large experience after a subtotal thyroidectomy, radioactive remnant ablation (RRA) at 30 years was shown to decrease recurrence rates (16% versus 38%) and death (3% versus 9%) when controlling for prognostic factors. However, multiple other studies have failed to show a benefit. A meta-analysis of >4,000 patients treated in 23 nonrandomized studies failed to show a benefit in overall survival; however, it did show an improvement in 10-year locoregional recurrence (relative risk 0.31) and an absolute 3% reduction in distant metastases with the addition of RRA.

Prior to RAI, administration of recombinant human thyrotropin or thyroid hormone withdrawal should be implemented to improve uptake of ^{131}I in remnant thyroid tissue or residual disease. Patients should also be given instructions for a low-iodine diet. Two recent, large, randomized trials demonstrated similar ablation rates after thyrotropin administration or thyroid hormone withdrawal, with 1 trial suggesting a trend toward increased adverse events with thyroid hormone withdrawal (30% versus 23%, P=.11) and the other trial showing a significantly higher proportion of patients with symptoms of hypothyroidism, deterioration of quality of life, and higher rates of lacrimal gland dysfunction after thyroid hormone withdrawal.

Based on these 2 studies, the use of recombinant human thyrotropin should be considered the preferred method to improve uptake of ^{131}I.

If a diagnostic scan is performed prior to therapy, ^{123}I should be administered to prevent stunning (the reduced uptake of subsequent RAI administration due to sublethal radiation damage) of thyroid tissue or residual disease. Alternatively, an empiric treatment dose of ^{131}I can be administered, making sure to obtain a post-treatment diagnostic scan. This should not be done if the results of the scan would change the therapeutic dose, per the American Thyroid Association (ATA) guidelines.

The dose for postoperative RAI remains controversial. Most centers use a fixed dose between 30 mCi and 100 mCi, depending on risk factors. A systematic review of 41 retrospective studies, 12 prospective studies, and 6 randomized studies compared the low dose (30 mCi) with the high dose (100 mCi) and found a trend toward improved ablation with the higher dose, although this did not reach significance. Multiple guidelines and recommendations have been released in recent years suggesting the use of ablative doses ranging from 30 mCi to 150 mCi. A recent study of patterns of care in North America showed that approximately 50% of centers treat with 100 mCi, 20% treat with 30 to 99 mCi, and 14% treat with ≤29.9 mCi for low-risk PTC. Two recent, large, randomized trials that included patients with pT1-3 and node-negative or -positive disease demonstrated equivalent rates of remnant ablation with 30 mCi and 100 mCi. ATA and National Comprehensive Cancer Network guidelines recommend 30 mCi to 100 mCi for patients without residual gross disease and 100 mCi to 200 mCi for patients with a high risk of local recurrence, residual gross disease, or distant metastases. These doses are similar to those used at large tertiary referral centers, including lower risk patients (age <45 years with intrathyroidal tumors <2 cm) receiving 30 mCi to 50 mCi, while intermediate-risk patients receive 75 mCi to 100 mCi for the initial therapy. Only patients with a high risk of local recurrence, residual gross disease, or distant metastases are treated with 130 mCi to 200 mCi. Whole body and blood dosimetry studies are rarely performed for routine RAI ablation, as the standard ^{131}I doses are well below a dose that may cause toxicity. Hospitalization is no longer required in most states following ^{131}I administration.

Toxicity associated with RAI includes transient parotitis, nausea, emesis, and bone marrow suppression. In 2 recent, large, randomized trials, longer post-treatment hospitalization stays, higher rates of adverse events, and decreased quality of life were significantly associated with a dose of 100 mCi compared with 30 mCi ^{131}I. Bone marrow suppression after a dose of 100 mCi for RRA has been shown to depress white blood cell and platelet counts at 1 year. There is no significant increased risk of infertility, spontaneous abortion, premature delivery, or congenital anomalies in children of women who receive RAI prior to pregnancy. To mitigate the potential adverse salivary effects of RAI, the use of pilocarpine and amifostine have been investigated. However, due to the cost and associated side effects, they are not used in standard practice. Most patients are advised to eat hard candies the day following RAI treatment to prevent accumulation of ^{131}I in the salivary glands. In the treatment of extensive metastatic disease, rare side effects include pulmonary fibrosis and an increase in malignancies, including leukemia and solid tumors.

Recent evidence shows an increase in RAI use for early-stage (pT1N0) thyroid cancer, with no evidence to support a survival outcome. This trend is of concern, given the known risk for second malignancies, particularly leukemia and salivary gland tumors.

Elderly patients should receive aggressive surgery (near-total or total thyroidectomy) followed by RAI if their performance status will tolerate it. A recent analysis of the Surveillance Epidemiology and End Results registry showed that elderly patients are less likely to be treated with surgery or RAI, although multivariable analysis associated both treatment modalities with improved survival.

External Beam Radiotherapy

The use of EBRT for thyroid cancer has not been tested in well-designed, randomized, controlled trials and should, therefore, be considered on a case-by-case basis following surgery and RAI. Indications for use of EBRT postoperatively can include gross residual disease, extracapsular or extrathyroidal extension, recurrent disease or ^{131}I failure, poor iodine avidity, multiple pathologically involved lymph nodes, HCC histology, patient age >45 years, or high risk on prognostic systems. There has been no report of successfully completed, randomized, controlled trials investigating the role of postoperative adjuvant EBRT. One trial attempted to randomize patients treated with surgery, ^{131}I, and TSH-suppression for pT4 FTC to EBRT for observation. Due to poor accrual, the trial became a prospective cohort study after only 45 of 311 patients had consented to randomization. Of the 47 randomized patients, 26 received EBRT. This trial failed to show a statistically significant local control benefit for EBRT, although there was a trend toward improved complete remission rates (96% versus 86%) and local control (100% versus 97%) with the addition of EBRT. Although there is a lack of prospective randomized data, retrospective evidence supports the use of EBRT in high-risk patients. A retrospective study of 169 patients with pathologic T4 disease who received RAI and TSH suppression therapy found a benefit with EBRT, which improved failure-free survival from 45% to 90%. However, this benefit was limited to patients >40 years of age with lymph node-positive disease. A similar benefit was not seen with FTC. Another study, in which 105 of 842 patients received EBRT, showed a benefit of EBRT use, with a relative risk of locoregional failure of 0.35. Although other studies failed to show a benefit to adjuvant EBRT after surgery and RAI, the groups receiving EBRT had unfavorable characteristics; therefore, selection bias may have played a role in this outcome. Based on the totality of the evidence, EBRT should be considered particularly for older patients (>40 years) with high-risk PTC or HCC (pathologic T4 or with pathologically involved lymph nodes) after surgery and RAI.

When administered postoperatively, EBRT treatment volumes for these patients usually include levels II–VII (including upper mediastinal lymph nodes) extending from the angle of the mandible to the tracheal bifurcation with or without the retropharyngeal lymph nodes at a dose of 45 to 50 Gy. The coverage of elective nodal regions is often recommended, based on small retrospective studies of locoregionally advanced nonanaplastic thyroid cancer that demonstrated significantly improved 5-year locoregional control (89% versus 40%) with the addition of elective field irradiation in the recurrent or postoperative setting with gross residual disease. No difference was seen in acute or late toxicities between the groups. High-risk microscopic regions (i.e., tumor bed, initial thyroid gland volume, adjacent primary nodal group, level VI, or any pathologically involved lymph node levels) are often treated with 60 Gy, while areas of positive margins are treated with 66 to 70 Gy. When treated, gross residual disease is often treated at 70 Gy or higher.

Conventional treatment fields traditionally consisted of anterior or anteroposterior/posteroanterior fields to below cord tolerance followed by anterior electrons or opposed lateral/oblique fields to the final dose. Interest is being directed at developing techniques to reduce EBRT-related toxicity, in particular intensity-modulated radiotherapy (IMRT). Recent publications have demonstrated the feasibility of using IMRT to treat patients with thyroid cancer. One group showed equivalent survival outcomes with reduced severe late morbidity (2% versus 12%) for ^{131}I postoperative patients when comparing 57 patients treated with IMRT to 74 patients treated with conventional radiotherapy.

When gross residual disease is present, some studies have suggested that EBRT may improve locoregional tumor control. For patients with an incomplete surgical resection, the addition of EBRT was shown to improve the 15-year local control from 77% to 89%, although the patients treated with EBRT had larger and more extensive tumors. Another study showed equivalent local control in patients treated with EBRT regardless of the extent of resection. Together, these studies demonstrate the potential effectiveness of EBRT. Risk factors that have been shown to predict for worse response to EBRT include high-risk histologic features, gross residual disease, and lack of iodine avidity.

Systemic Therapy

Chemotherapy plays a minimal role in the management of WDTC. Doxorubicin is currently the only U.S. Food and Drug Administration (FDA)-approved agent for noniodine avid disease. Studies are now elucidating the common genetic alterations in thyroid cancer such as the BRAF gene V600E mutation, which may represent targets for novel biologic agents. Similarly, vascular endothelial growth factor (VEGF) is overexpressed in WDTC, which has prompted the study of small molecule tyrosine kinase inhibitors over the past few years. Sorafenib has demonstrated response rates of 15% to 23% in 3 phase II studies. Axitinib and pazopanib have also been evaluated with similar results. In a multi-institutional phase II study, lenvatinib demonstrated a response rate of 50%, with a median progression-free survival (PFS) rate of 13 months, and recently it was compared to a placebo in a large, randomized, phase III trial, the results of which are pending. The results of the DECISION trial—a multi-institutional, randomized, placebo-controlled, phase III trial comparing sorafenib with a placebo—were presented at the 2013 American Society of Clinical Oncology Annual Meeting. In evaluation of the primary endpoint of this study, sorafenib demonstrated an improvement over the placebo in the PFS rate by 5 months, and the majority of adverse events were manageable and nonlife threatening. The objective response rate for sorafenib was 23%, and survival was not improved due to the cross-over effect in the placebo arm. Interestingly, at 400 days 25% of the placebo arm patients did not demonstrate disease progression, begging the question of whom to treat and when. In 1 series of WDTC patients, who were iodine-refractory and FDG-negative, the median PFS rate was 41 months without treatment. Deciding when and to whom to administer targeted therapy may become more evident as data from a subset analysis of this study and future randomized studies evolve. Additional data suggest that targeting molecular phenotypes may also be reasonable. A recent study demonstrated that radioiodine uptake could be enhanced by selumetinib in advanced thyroid cancer patients. Similarly, vemurafenib may induce clinical responses in patients harboring BRAF mutations. (See Variants 1, 2, and 3, above.)

Well-Differentiated Thyroid Cancer—Medullary Thyroid Cancer

MTC is a neuroendocrine tumor of the parafollicular C cells, which produce calcitonin. Approximately 80% of MTC cases are sporadic, although some are familial, arising from multiple endocrine neoplasia type 2 (MEN2) syndrome. The management of patients with MEN2 syndrome should include familial screening and evaluation for a prophylactic thyroidectomy. Further discussion is beyond the scope of this review. At the time of diagnosis, approximately 50% of patients with MTC have clinically detectable cervical lymph node metastases. All patients with sporadic MTC should be offered germline RET oncogene testing, given that approximately 6% to 7% of unselected patients with MTC have a germline mutation.

The primary management for MTC is surgical resection with a lymphadenectomy. Prior to surgery, all patients with MTC should be evaluated for pheochromocytoma, or, to rule out pheochromocytoma, they should be tested for a negative RET proto-oncogene mutation and have a negative family history for MTC. Staging is based on size, extrathyroidal extension, lymph node status, and metastases. There is no role for RAI, as MTC is not iodine avid. Thyroxine should be started immediately following surgery with the goal of maintaining euthyroidism. There is no role for suppression of serum thyrotropin, because parafollicular C cells do not respond to TSH. EBRT is recommended postoperatively for patients with gross residual disease to obtain local control. In a series of 21 patients treated postoperatively with gross residual disease, local control was 20%, which is poor but demonstrates that local control can be achieved in a subset of patients. The use of adjuvant EBRT for microscopic disease is less clear. There have been no reports of a consistent survival benefit with the use of adjuvant EBRT, likely due to microscopic disease outside of the

neck. However, local control improves with the use of EBRT. In 1 series of 40 patients with high-risk features, including gross residual disease, positive lymph nodes, or extracapsular extension, the use of postoperative adjuvant EBRT (median 40 Gy) significantly improved 10-year local-regional control (86% versus 52%). In another series of 51 patients with elevated postoperative calcitonin, 24 were treated with EBRT; local control was 71% versus 41% favoring EBRT, although this was not statistically significant. Additionally, a series of 34 patients with stage IVa-c disease treated with EBRT (median 60 Gy) showed a local control rate of 87%, confirming the role for adjuvant EBRT in locally extensive disease. The recommended dose for EBRT is 56 Gy to cervical lymph nodes, 66 Gy to areas concerning microscopic residual disease, and >70 Gy for gross disease. Patients are followed with regular serum calcitonin and carcinoembryonic antigen measurements to detect recurrence. In the recurrent setting, EBRT should be considered after the surgical resection of a locoregional recurrence or for palliation of a symptomatic distant metastasis. Therefore, when locoregional control is important, consideration should be given for EBRT use.

Metastatic MTC is difficult to treat. Chemotherapy provides minimal benefit. Recently, the FDA approved vandetanib for the treatment of symptomatic or progressive MTC in patients with unresectable, locally advanced, or metastatic disease. Vandetanib is the first drug approved for this indication. Approval was based on the results of a double-blind trial, in which patients were randomized 2:1 to vandetanib (300 mg/d orally) versus a placebo. The primary objective was to demonstrate improvement in PFS with vandetanib compared with the placebo. Other endpoints included evaluation of the overall survival and objective response rates. The PFS analysis showed a marked improvement for patients randomized to vandetanib (hazard ratio = 0.35; 95% confidence interval, 0.24–0.53; P<.0001). The objective response rate for the vandetanib arm was 44% compared with 1% for the placebo arm. Cabozantinib, a potent dual inhibitor of the mesenchymal-epithelial transition (MET) and VEGF pathways designed to block MET-driven tumor escape, has also shown promise in a recently reported, randomized, placebo-controlled study in patients with progressive metastatic MTC. (See Variant 4, above.)

Anaplastic Thyroid Cancer

Patients with ATC have a uniformly poor prognosis. ATC is a locally aggressive disease process frequently involving the regional lymph nodes, perithyroidal fat, neck musculature, larynx, trachea, esophagus, and vasculature of the neck and mediastinum. Given the rapidly growing and infiltrative nature of ATC, aggressive local therapy is often recommended, although there is no randomized evidence to support this approach. Distant metastases are present in ≤50% of newly diagnosed cases, most commonly to the lungs. In addition to locoregional treatment, end-of-life issues and palliative care should be addressed early in the disease process. Diagnostic studies should include CT of the neck and chest to evaluate for local extent and distant metastases to the lungs. Fine needle aspiration or surgical biopsy should be done to confirm the diagnosis. Given the rarity of this tumor, data are limited, with no randomized controlled trials to support treatment recommendations. Patient age (<60 years) and an intrathyroidal tumor have been shown to be favorable prognostic factors.

Surgery is only indicated if imaging shows the disease is localized to the thyroid, although this is uncommon given the locally aggressive nature of ATC. However, some studies have shown long-term survival after the surgical resection of intrathyroidal tumors. A thyroid lobectomy with adequate margins is appropriate for resectable disease, as more aggressive surgery, including total thyroidectomy, is associated with increased complications and no improvement in survival. Unlike WDTC, thyroglobulin levels are not used to monitor for recurrence or metastasis in ATC, making total thyroidectomy unnecessary for follow-up purposes. The addition of radiation to surgery has been shown in a Surveillance, Epidemiology, and End Results analysis to improve survival in patients with disease extending into adjacent tissue but not in those with disease confined to the thyroid or those with distant metastases. Multiple retrospective series have shown a benefit to adjuvant radiation after surgery.

Adjuvant combined modality therapy, including radiation and chemotherapy, has been shown to improve outcomes for ATC patients. One study used surgery (when feasible) followed by IMRT and 4 cycles of docetaxel and doxorubicin to treat 10 patients with regionally localized disease. Two patients were hospitalized for treatment-related complications. The median survival for the group was 60 months, which compares favorably with historical outcomes. Another group reviewed 33 patients with ATC and found that ATC treated with a complete resection followed by adjuvant chemoradiation had a median survival of 5 months.

The optimal sequencing of therapeutic modalities for ATC patients is not known and is usually decided on a case-by-case basis. One study evaluated the timing of sequential therapy. Seventy-nine patients with ATC were divided into surgery up front (n=26) versus chemotherapy and/or radiotherapy (n=53). The latter group included 12 patients who underwent surgery after induction therapy. No difference in survival was found between the groups, although the primary concurrent chemoradiation group was older, had larger tumors not confined to the thyroid, and had a higher rate of regional metastases. The best outcome was seen in patients who received primary concurrent chemoradiation followed by surgery (the 1-year survival rate was 50%). Another study reported a complete response rate of 25% and a median survival rate of 11 months in patients treated with a combination of total thyroidectomy, chemotherapy, and radiation.

Management of ATC that is unresectable at diagnosis is controversial. Radiotherapy alone in conventional fractionation does not prolong survival. One study showed an 80% initial response rate, but most patients developed a local recurrence. Neoadjuvant hyperfractionated radiotherapy combined with radiosensitizing chemotherapy followed by surgery (if feasible) was reported to have an overall survival rate of approximately 12 months, with distant metastasis then becoming the predominant mode of failure. Chemoradiation with standard fractionation in the definitive setting

has been reported to provide promising survival outcomes.

Altered radiation fractionation has been explored as another method to improve outcomes in ATC. Early reports of hyperfractionated EBRT showed some tumor responses, but there was limited interest due to a significant risk of radiation myelopathy. However, improved planning and treatment delivery techniques have renewed interest in altered fractionation for ATC. Comparisons of standard radiation fractionation regimens to hyperfractionated radiation without chemotherapy have failed to show significant benefits in survival, although 1 study did show a nonsignificant (P=.3) trend toward improved survival with hyperfractionated radiotherapy.

Promising outcomes have also been reported for altered radiation fractionation combined with chemotherapy and surgery (if feasible) for locally advanced ATC, although there are no randomized prospective studies evaluating this treatment modality. One recent series reported on 10 patients treated with IMRT (7 of 10 had altered fractionation, with a median dose of 64.25 Gy) and concurrent and adjuvant chemotherapy. One- and 2-year overall survival rates were promising at 70% and 60%, respectively. One group prospectively reported 30 patients (24 had undergone resection) treated sequentially with 2 cycles of doxorubicin and cisplatin, radiotherapy in 1.25-Gy fractions twice daily to a dose of 40 Gy (field extended from mastoid to carina) with a boost to 50 to 55 Gy, and then 4 cycles of doxorubicin and cisplatin. A total of 19 patients had a complete response to therapy, although there was a high rate of hematologic and pharyngoesophageal toxicity. Outcomes were promising, with a 3-year overall survival rate of 27%. Six of 7 long-term survivors underwent a macroscopic complete resection. On multivariable analysis, tracheal extension and macroscopic complete resection were significant predictors of survival. Another group reported on 22 patients treated with hyperfractionated radiotherapy (1.6 Gy twice daily) to a total dose of 46 Gy, with concurrent weekly doxorubicin followed by surgery 2 to 3 weeks after completing radiation and then additional weekly doxorubicin, if tolerated. Seventeen of the 22 patients proceeded to operation and none developed a local recurrence, although the median overall survival for this group was only 2 months. This raises the question of possible treatment-related morbidity and mortality. Another series reported on 19 patients treated with concurrent doxorubicin and a radiotherapy dose of 57.6 Gy (1.6 Gy fractions twice daily, 3 days per week). A complete response was observed in 84% of patients with local control of 68% at 2 years. The median survival rate was 1 year, with most patients dying of metastatic disease.

There is limited evidence for a radiation dose response in ATC. One study reported a survival benefit in patients who received >50 Gy, and another showed an improvement in PFS if the radiation dose was >40 Gy.

Treatment fields should include the thyroid or thyroid bed and adjacent lymph node echelons in the neck and mediastinum. There are no data to support treating the entire neck and mediastinum. Dose fractionation schemes are variable, but 60 Gy in 1.5 Gy fractions twice daily is an appropriate and accepted fractionation scheme. For patients with poor performance status or metastatic disease, a palliative regimen of 20 Gy in 4-Gy fractions or 30 Gy in 3-Gy fractions should be considered to slow local progression. Some groups treat with 20 Gy in 4-Gy fractions, with a second course of 20 Gy 4 weeks later in patients who show a response to treatment.

As with other thyroid cancer variants, IMRT is being actively explored as a method to reduce toxicity and improve the therapeutic ratio. One retrospective study compared toxicity in patients treated with either IMRT or 3-D conformal EBRT. No difference in toxicity was reported, which was attributed to the wide field coverage used for IMRT.

Overall, for locally advanced ATC, aggressive combined modality therapy (surgery if localized to the thyroid, chemotherapy, and radiation) has been attempted with mixed results. However, given the locally aggressive nature of ATC, aggressive local therapy is recommended to prevent or delay death by local progression (see Variants 5 and 6, above).

Metastatic Thyroid Cancer

Management of metastatic thyroid cancer depends on the histologic variant. Patients with metastatic WDTC may still benefit from local control, given the ability of RAI to eradicate distant disease. Patients with tumors that do not uptake iodine have a worse prognosis. When managing patients with extracervical metastases from thyroid cancer, the goals should be to improve survival, palliate symptoms, prevent morbidity, and limit treatment-related toxicity. If the tumor remains iodine-avid, RAI should be attempted with a dose of 150 mCi to 200 mCi. Patients with pulmonary metastases should receive a dose of 150 mCi to reduce the risk of pulmonary toxicity. One series of 444 patients, 295 of whom had iodine-avid metastatic disease, showed a 43% rate of resolution of iodine-avid metastases. The 10-year survival rate was 92% for the group with resolution of RAI avidity compared with 19% in disease that did not completely resolve.

EBRT should be used to palliate local symptoms that are not amenable to RAI or require rapid relief. Lesion positron emission tomography (PET) avidity is inversely correlated with iodine avidity; therefore, PET-avid lesions should be treated with EBRT, as they do not respond to ^{131}I therapy. Dose regimens of 8 Gy in a single fraction, 20 Gy in 5 fractions, 30 Gy in 10 fractions, or 37.5 Gy in 15 fractions are all appropriate.

Novel biologic agents, such as systemic therapy options, are being actively investigated. The tyrosine kinase inhibitor axitinib has shown a 30% overall response rate in incurable thyroid cancer of any histology, and thalidomide has shown activity in rapidly progressive metastatic thyroid cancer. Patients with metastatic thyroid cancer that is not iodine avid should be encouraged to enroll in clinical trials that further explore novel

systemic agents (see Variants 7 and 8, above).

Summary

- For WDTC, surgery and often adjuvant RAI are common components of therapy.
- The role of radiotherapy is less well defined and is often decided on a case-by-case basis.
- Systemic therapeutic options, particularly with targeted therapies, are being actively investigated.
- ATCs usually require a multimodality approach, typically with concurrent chemotherapy and radiation.

Abbreviations

- 3-D, 3-dimensional
- CRT, conformal radiation therapy
- IMRT, intensity-modulated radiation therapy
- LN, lymph node
- RAI, radioactive iodine
- RRA, radioactive remnant ablation

Clinical Algorithm(s)

Algorithms were not developed from criteria guidelines.

Scope

Disease/Condition(s)

Thyroid carcinoma

Guideline Category

Management

Treatment

Clinical Specialty

Endocrinology

Nuclear Medicine

Oncology

Radiation Oncology

Radiology

Surgery

Intended Users

Health Plans

Hospitals

Managed Care Organizations

Physicians

Utilization Management

Guideline Objective(s)

To evaluate the appropriateness of treatment procedures for thyroid carcinoma

Target Population

Patients with thyroid carcinoma

Interventions and Practices Considered

1. Total lobectomy (hemithyroidectomy)
2. Total thyroidectomy
3. Lateral lymph node dissection
4. Thyroglobulin suppression with levothyroxine
5. Postoperative adjuvant radioactive iodine (radioactive remnant ablation [RRA] or radioactive iodine [RAI])
    - With thyrotropin stimulation
    - With thyroid hormone withdrawal
    - After total thyroidectomy
    - After subtotal thyroidectomy
6. Postoperative chemotherapy
7. Adjuvant concurrent chemoradiotherapy
8. Postoperative external beam radiotherapy (EBRT)
    - 3-dimenstional conformal radiation therapy (3D-CRT)
    - Intensity-modulated radiation therapy (IMRT)
    - Treating thyroid bed first echelon lymph nodes only
    - Treating thyroid bed and entire elective neck
    - Altered fractionation
    - Postoperative concurrent chemoradiotherapy
    - Definitive chemoradiotherapy (if no surgery performed)
9. Genetic testing for family members
10. Palliative chemotherapy alone
11. Cytotoxic chemotherapy
12. Palliative EBRT
13. Tyrosine kinase inhibitor (TKI) therapy

Major Outcomes Considered

- Recurrence rate
- Morbidity and mortality
- Survival rate
- Detection of distant metastases
- Treatment-related toxicity and complications

Methodology

Methods Used to Collect/Select the Evidence

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search Procedure

Staff will search in PubMed only for peer reviewed medical literature for routine searches. Any article or guideline may be used by the author in the narrative but those materials may have been identified outside of the routine literature search process.

The Medline literature search is based on keywords provided by the topic author. The two general classes of keywords are those related to the condition (e.g., ankle pain, fever) and those that describe the diagnostic or therapeutic intervention of interest (e.g., mammography, MRI).

The search terms and parameters are manipulated to produce the most relevant, current evidence to address the American College of Radiology Appropriateness Criteria (ACR AC) topic being reviewed or developed. Combining the clinical conditions and diagnostic modalities or therapeutic procedures narrows the search to be relevant to the topic. Exploding the term "diagnostic imaging" captures relevant results for diagnostic topics.

The following criteria/limits are used in the searches.

1. Articles that have abstracts available and are concerned with humans.
2. Restrict the search to the year prior to the last topic update or in some cases the author of the topic may specify which year range to use in the search. For new topics, the year range is restricted to the last 10 years unless the topic author provides other instructions.
3. May restrict the search to Adults only or Pediatrics only.
4. Articles consisting of only summaries or case reports are often excluded from final results.

The search strategy may be revised to improve the output as needed.

Number of Source Documents

The total number of source documents identified as the result of the literature search is not known.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Strength of Evidence Key

Category 1 - The conclusions of the study are valid and strongly supported by study design, analysis and results.

Category 2 - The conclusions of the study are likely valid, but study design does not permit certainty.

Category 3 - The conclusions of the study may be valid but the evidence supporting the conclusions is inconclusive or equivocal.

Category 4 - The conclusions of the study may not be valid because the evidence may not be reliable given the study design or analysis.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The topic author drafts or revises the narrative text summarizing the evidence found in the literature. American College of Radiology (ACR) staff draft an evidence table based on the analysis of the selected literature. These tables rate the strength of the evidence (study quality) for each article included in the narrative text.

The expert panel reviews the narrative text, evidence table, and the supporting literature for each of the topic-variant combinations and assigns an appropriateness rating for each procedure listed in the table. Each individual panel member assigns a rating based on his/her interpretation of the available evidence.

More information about the evidence table development process can be found in the ACR Appropriateness Criteria® Evidence Table Development document (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

Description of Methods Used to Formulate the Recommendations

Rating Appropriateness

The appropriateness ratings for each of the procedures included in the Appropriateness Criteria topics are determined using a modified Delphi methodology. A series of surveys are conducted to elicit each panelist's expert interpretation of the evidence, based on the available data, regarding the appropriateness of an imaging or therapeutic procedure for a specific clinical scenario. American College of Radiology (ACR) staff distribute surveys to the panelists along with the evidence table and narrative. Each panelist interprets the available evidence and rates each procedure. The surveys are completed by panelists without consulting other panelists. The appropriateness rating scale is an ordinal scale that uses integers from 1 to 9 grouped into three categories: 1, 2, or 3 are in the category "usually not appropriate"; 4, 5, or 6 are in the category "may be appropriate"; and 7, 8, or 9 are in the category "usually appropriate." Each panel member assigns one rating for each procedure for a clinical scenario. The ratings assigned by each panel member are presented in a table displaying the frequency distribution of the ratings without identifying which members provided any particular rating.

If consensus is reached, the median rating is assigned as the panel's final recommendation/rating. Consensus is defined as eighty percent (80%) agreement within a rating category. A maximum of three rounds may be conducted to reach consensus. Consensus among the panel members must be achieved to determine the final rating for each procedure.

If consensus is not reached, the panel is convened by conference call. The strengths and weaknesses of each imaging procedure that has not reached consensus are discussed and a final rating is proposed. If the panelists on the call agree, the rating is proposed as the panel's consensus. The document is circulated to all the panelists to make the final determination. If consensus cannot be reached on the call or when the document is circulated, "No consensus" appears in the rating column and the reasons for this decision are added to the comment sections.

This modified Delphi method enables each panelist to express individual interpretations of the evidence and his or her expert opinion without excessive influence from fellow panelists in a simple, standardized and economical process. A more detailed explanation of the complete process can be found in additional methodology documents found on the ACR Web site (see also the "Availability of Companion Documents" field).

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The recommendations are based on analysis of the current literature and expert panel consensus.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Selection of appropriate treatment procedures for thyroid carcinoma

Potential Harms

- Two recent, large, randomized trials demonstrated similar ablation rates after thyrotropin administration or thyroid hormone withdrawal, with 1 trial suggesting a trend toward increased adverse events with thyroid hormone withdrawal (30% versus 23%, P=.11) and the other trial showing a significantly higher proportion of patients with symptoms of hypothyroidism, deterioration of quality of life, and higher rates of lacrimal gland dysfunction after thyroid hormone withdrawal.
- A thyroid lobectomy with adequate margins is appropriate for resectable disease, as more aggressive surgery, including total thyroidectomy, is associated with increased complications and no improvement in survival.
- Completion thyroidectomy for recurrent disease has a high associated morbidity (due to the resulting total thyroidectomy, with increased risks to the laryngeal nerves and parathyroid glands).
- Toxicity associated with radioactive iodine (RAI) includes transient parotitis, nausea, emesis, and bone marrow suppression. Most patients are advised to eat hard candies the day following RAI treatment to prevent accumulation of ^{131}I in the salivary glands. In the treatment of extensive metastatic disease, rare side effects include pulmonary fibrosis and an increase in malignancies, including leukemia and solid tumors.
- Combining altered radiation fractionation with chemotherapy resulted in a high rate of hematologic and pharyngoesophageal toxicity in one reported study.
- Intensity-modulated radiation therapy (IMRT) is being actively explored as a method to reduce toxicity and improve the therapeutic ratio. One retrospective study compared toxicity in patients treated with either IMRT or 3-dimensional (3-D) conformal external beam radiation therapy (EBRT). No difference in toxicity was reported, which was attributed to the wide field coverage used for IMRT.

Contraindications

Contraindications

Radioactive iodine (RAI) should not be given to pregnant women due to the theoretical risk to the fetus.

Qualifying Statements

Qualifying Statements

The American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Salama JK, Golden DW, Beitler JJ, Yom SS, Garg MK, Lawson J, McDonald MW, Quon H, Ridge JA, Saba N, Smith RV, Worden F, Yeung AR, Expert Panel on Radiation Oncologyâ€“Head & Neck Cancer. ACR Appropriateness CriteriaÂ® thyroid carcinoma. [online publication]. Reston (VA): American College of Radiology (ACR); 2013. 18 p. [100 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2013

Guideline Developer(s)

American College of Radiology - Medical Specialty Society

Source(s) of Funding

The American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

Guideline Committee

Committee on Appropriateness Criteria, Expert Panel on Radiation Oncology–Head & Neck Cancer

Composition of Group That Authored the Guideline

Panel Members: Joseph K. Salama, MD (*Principal Author*); Daniel W. Golden, MD (*Research Author*); Jonathan J. Beitler, MD, MBA (*Panel Chair*); Sue S. Yom, MD, PhD (*Panel Vice-chair*); Madhur Kumar Garg, MD; Joshua Lawson, MD; Mark W. McDonald, MD; Harry Quon, MD, MS; John A. Ridge, MD, PhD; Nabil Saba, MD; Richard V. Smith, MD; Francis Worden, MD; Anamaria Reyna Yeung, MD

Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the American College of Radiology (ACR) Web site.

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

Availability of Companion Documents

The following are available:

- ACR Appropriateness Criteria®. Overview. Reston (VA): American College of Radiology; 2013 Nov. 3 p. Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.
- ACR Appropriateness Criteria®. Literature search process. Reston (VA): American College of Radiology; 2013 Apr. 1 p. Electronic copies: Available in PDF from the ACR Web site.
- ACR Appropriateness Criteria®. Evidence table development – diagnostic studies. Reston (VA): American College of Radiology; 2013 Nov. 3 p. Electronic copies: Available in PDF from the ACR Web site.
- ACR Appropriateness Criteria®. Evidence table development – therapeutic studies. Reston (VA): American College of Radiology; 2013 Nov. 4 p. Electronic copies: Available in PDF from the ACR Web site.
- ACR Appropriateness Criteria® thyroid carcinoma. Evidence table. Reston (VA): American College of Radiology; 2013. 36 p. Electronic copies: Available from the ACR Web site.

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on March 12, 2014.

Copyright Statement

Disclaimer

NGC Disclaimer

The National Guideline Clearinghouseâ„¢ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria.

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.